Phosphorylation along the electron transport chain has a very different explanation, as first outlined in the chemiosmotic hypothesis of Peter Mitchell (1961; 1966). Now called *oxidative phosphorylation*, this process turned out to depend upon the presence and structure of the inner membrane of the mitochondrion. The energy used to drive oxidative phosphorylation is stored, not in a chemical intermediate, but rather in a proton gradient across the membrane. With the eventual acceptance of this hypothesis, there no longer was any need to find the hypothesized chemical intermediate. Much more relevant were discoveries concerning the inner structure of the mitochondrion and the dependence of certain biochemical processes on that structure. These developments resulted from the interaction of biochemists and morphologists during the 1950s, which will be the focus of this section.

While Claude, Hogeboom, and their colleagues were making progress at the Rockefeller Institute, at the University of Chicago Albert Lehninger and his graduate student Eugene Kennedy were also conducting biochemical studies on particulate structures fractionated from rat liver. They, however, targeted the oxidation of fatty acids rather than carbohydrates. In ordinary liver preparations, a complex enzyme system catalyzes oxidation of the fatty acid octanoate (octanoic acid) via two possible pathways, one producing ketone bodies such as acetoacetate (acetoacetic acid) and the other proceeding through the citric acid cycle and respiratory chain, producing CO_2 and consuming oxygen to generate H_2O. Prior to Hogeboom et al.'s introduction of isotonic sucrose solution, Schneider, who was then still a graduate student at Wisconsin, had collaborated with Lehninger in testing a mitochondrial fraction of liver for evidence of fatty acid oxidation. Schneider tried supplying both water and saline suspensions of the mitochondrial fraction with octanoate and necessary supplementary substances (KCl, $MgSO_4$, a "sparking" Krebs intermediate, cytochrome *c*, phosphate buffer, ATP), but found no significant oxidation. Instead, he found oxidation occurring primarily in a fraction containing nuclei, erythrocytes, and some intact cells. After Hogeboom et al.'s (1948) paper, Lehninger set Kennedy to repeating this earlier work. Kennedy showed that with 0.88 *M* sucrose as the fractionation medium, octonoate oxidation occurred in the mitochondrial fraction (Kennedy & Lehninger, 1949).

previously hypothesized, but rather in substrate phosphorylation. Likewise, Boyer formulated an alternative mechanism of oxidative phosphorylation involving conformational changes that he initially advanced against both the chemical intermediate view and Mitchell's chemiosmotic view. He later recognized that his proposal was in fact compatible with Mitchell's account if he limited its scope to the actual synthesis of ATP. These efforts ultimately brought Boyer a Nobel Prize, even though his success did not lie in identifying the central mechanism of oxidative phosphorylation.